REMARKS

Claims 13-29 are pending in the application. Claims 13-22 are withdrawn from consideration. Claims 23-28 are rejected. Claim 29 is objected to.

Response to Claim Rejections under 35 USC §112, First Paragraph

Claims 23-28 are rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement.

Claim 23

The Examiner previously raised concerns with regard to support in the specification for the term "adjacent". In the previous Response, Applicants amended claim 23 to replace "adjacent" with "proximal", a term expressly finding support in the specification. The Examiner recognizes that the specification provides support for the term "proximal" but continues to find such support to be only in the context of the 200 base pair promoter sequence proximal to the start codon of the *relA/SpoT* codinq sequence. In the Examiner's view, claim 23, as amended, now reads on any 200 base pair sequence upstream and proximal to the *Mycobacterium tuberculosis relA/SpoT* gene while the instant specification provides support for only the 200 bp sequence upstream and proximal to the start codon and specifically the sequence of SEQ ID NO:2.

Applicants respectfully submit that one skilled in the art would understand that claim 23 as previously amended, when properly read in light of the specification, would not read on *any* base pair sequence but to the sequence as disclosed in the present application. Nonetheless for purposes of clarification and advancing prosecution, claim 23 has been amended to recite that the 200 bp promoter fragment is located proximal to the start codon of the *Mycobacterium tuberculosis* relA/SpoT coding sequence.

Withdrawal of the rejection under 35 U.S.C. § 112 is respectfully requested.

Response to Claim Rejections under 35 U.S.C. § 103

Claim 23

Claim 23 is rejected under 35 U.S.C. §§103 as allegedly being unpatentable over Avarbock et al. ("Avarbock") in view of Ojha et al. ("Ohja").

The Examiner finds that Avarbock teaches 1) the cloning and characterization of the *relA/SpoT* homologue in *M. tuberculosis*; 2) the cloning of the upstream and downstream sequences of the *relA/SpoT* homologue in *M. tuberculosis* (see Fig. 2); and 3) comparison of the gene organization of the *rel* locus in *M. tuberculosis* with that of multiple other organisms. The Examiner contends that Avarbock indicates that the *relA/SpoT* promoter appears to be located in the intergenic region immediately upstream of the *relA/SpoT* coding region and in the upstream *apt* gene but recognizes that Avarbock does not provide a rationale for isolating the promoter of the *relA/SpoT* gene.

The Examiner relies on Ojha for providing a rationale for isolating the promoter. Ojha teaches that the *relA/SpoT* gene products are involved in production of ppGpp, that ppGpp may play an important role in latency in mycobacteria and that studies on the stringent pathways (involving accumulation of ppGpp) may be important in understanding the transformation of avirulent to virulent forms of *M. tuberculosis*. The Examiner relies on Avarbock to assert that a 200 bp fragment of the proximal upstream region would have been the obvious promoter region.

The Examiner also states that Avarbock teaches that in other species promoters of relA/SpoT genes are found within the approximately 200 bases upstream of the coding region, that Avarbock indicates that the promoter *M.tuberculosis relA/SpoT* gene is within the 30 bp intergenic region between the *relA/SpoT* gene and the *apt* gene and that readthrough transcription

from the *apt* gene probably occurs in *M.tuberculosis* since readthrough transcription occurs in *S.coelicolor rel.*

Based on the above contentions, the Examiner concludes that one of ordinary skill would have been motivated to isolate the *M. tuberculosis relA/SpoT* promoter in the 200 base pair upstream proximal region to the *relA/SpoT* ORF and asserts that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Applicants respectfully disagree with the Examiner's analysis. With respect to *M. tuberculosis,* Avarbock does not indicate that the *relA/SpoT* promoter appears to be located in the intergenic region immediately upstream of the *relA/SpoT* coding region. Rather, that indication applies to *S. coelicolor*. As for *M. tuberculosis,* Avarbock seems to indicate that the promoter does not map to the intergenic region (see p. 266, Discussion, first paragraph). Further, Avarbock discloses that transcription of *S. coelicolor* occurs from multiple promoters, two within a 182 bp *apt-rel* intergenic region and a third corresponding to transcriptional readthrough from *apt.* The location for the *apt* promoter however is not disclosed. Indeed, the point of origination of transcriptional readthrough may be beyond 200 bp. Further still, Avarbock suggests only that *transcriptional readthrough* may occur in *M. tuberculosis*; Avarbock does not teach or suggest the location of the *relA* or *apt* promoters in *M. tuberculosis*, let alone render the 200 bp proximal upstream region the obvious promoter region.

Applicants respectfully submit that Avarbock does not suggest a 200 bp fragment of the proximal upstream region as an obvious promoter region and that the combination of Avarbock and Ojha neither teaches nor suggests the promoter of claim 23.

Withdrawal of the rejection under 35 U.S.C. § 103 is respectfully requested.

Claims 24-28

Claims 24-28 are rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Avarbock in view of Ojha as applied to claim 23 above, and further in view of Hemming et al.

Applicants submit that the present amendment and remarks provided with respect to claim 23 are believed to render the rejection of dependent claims 24-28 moot.

Response to Claim Objections

Claim 29

Claim 29, wherein the promoter consists of SEQ ID NO: 2, is objected to as being dependent upon a rejected base claim. Claim 29 has been rewritten in independent form.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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Date: July 28, 2008